

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of modulating splice site selection and splicing thereof, said method comprising the step of hybridizing an oligonucleotide-~~protein conjugate~~ to a target pre-mRNA molecule in a cell or cell extract, wherein said oligonucleotide-~~protein conjugate~~ comprises ~~an oligonucleotide~~ a moiety capable of binding to a protein moiety, ~~and which~~ comprises at least two distinct sequence elements:
 - (i) a nucleic acid sequence that is complementary to a specific region upstream of said splice site in said target pre-mRNA molecule; and
 - (ii) an extension containing a protein binding site sequence element for ~~covalently~~ binding a protein moiety; andwherein said protein moiety comprises a protein capable of modulating splicing of said splice site upon binding with said protein binding site.
2. (Currently amended) The method of claim 1, wherein said binding of said protein moiety is effected prior to hybridizing of said oligonucleotide ~~moiety~~ to said target pre-mRNA molecule or thereafter.
3. (Original) The method of claim 1, wherein said modulating is one of increasing or repressing splice site selection and splicing thereof.
4. (Original) The method of claim 1, wherein said splice site is a 5' splice site.
5. (Original) The method of claim 1, wherein said splice site is a 3' splice site.
6. (Original) The method of claim 1, wherein said cell is a mammalian cell.

7. (Previously presented) The method of claim 1, wherein said cell is in a patient.

8-27. (Cancelled)

28. (Original) The method of claim 1, wherein said oligonucleotide moiety is having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 to SEQ ID NO:14 and SEQ ID NO:18 to SEQ ID NO:33.

29-84. (Cancelled)

85. (Currently amended) An oligonucleotide moiety for modulating splice site selection and splicing thereof in a target pre-mRNA molecule present in a cell or cell extract, which comprises at least two distinct sequence elements:

- (i) a nucleic acid sequence that is complementary to a specific region upstream of said splice site in said target pre-mRNA molecule; and
- (ii) an extension containing a protein binding site sequence element for ~~covalently~~ binding a protein.

86. (Original) The oligonucleotide moiety of claim 85, wherein said extension is 5' CGU ACA CCA UCA GGG UAC-3' (SEQ ID NO: 1).

87. (Previously presented) The oligonucleotide moiety of claim 85, wherein said oligonucleotide moiety is comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 to SEQ ID NO:14 and SEQ ID NO:18 to SEQ ID NO:33.

88-103. (Cancelled)

104. (Previously presented) A method of creating an alternate form of mRNA or an alternate form of a protein comprising the steps of administering to a cell or a cell extract a sufficient amount of the oligonucleotide moiety of of claim 85 and administering to said

cell or said cell extract a purified protein capable of binding to said protein binding site.

105-106. (Cancelled)

107. (Previously presented) A method of reducing and/or inhibiting expression of an mRNA molecule or protein, said method comprising the step of administering to a cell or a cell extract a sufficient amount of the oligonucleotide moiety of of claim 85 and administering to said cell or said cell extract a purified protein capable of binding with said protein binding site.

108. (Previously presented) A method of reducing and/or inhibiting neuronal differentiation, said method comprising the steps of administering to a cell or a cell extract a sufficient amount of the oligonucleotide moiety of of claim 85 and administering to said cell or said cell extract a purified protein capable of binding with said protein binding site.

109. (Previously presented) A method of preventing a viral infection in a patient, said method comprising the step of administering a therapeutically effective amount of the oligonucleotide moiety of of claim 85 and a therapeutically effective amount of a purified protein capable of binding with said protein binding site to said patient.

110-115. (Cancelled)

116. (Previously presented) A method for treating a disease resulting from a mutation leading to aberrant splicing in a patient, said method comprising the steps of administering a therapeutically effective amount of the oligonucleotide moiety of of claim 85 and a therapeutically effective amount of a purified protein capable of binding to said protein binding site to said patient.

117. (Original) The method of claim 116, wherein said disease is selected from the group consisting of β -thalassemia, cystic fibrosis, haemophilia, retinoblastoma, analbuminemia, Lesch-Nyhan syndrome, acute intermittent porphyria, breast and ovarian cancer, carbohydrate-deficient glycoprotein syndrome type 1a, cerbrotendinous xanthomatosis, Ehlers-Danlos syndrome type VI, Fanconi anemia, frontotemporal dementia, HPRT deficiency, Leigh's encephalomyelopathy, Marfan syndrome, metachromatic leukodystrophy (juvenile form), neurofibromatosis type 1, OCT deficiency, porphyria cutanea tarda, Sandhoff disease, severe combined immunodeficiency, spinal muscle atrophy, tyrosinemia type 1, and Duchenne muscular dystrophy.
- 118-122. (Cancelled)
123. (Previously presented) A method for promoting cell death in a patient, said method comprising the steps of administering an effective amount of the oligonucleotide moiety of claim 85 and an effective amount of a purified protein capable of binding to said protein binding site to said patient.
- 124-129. (Cancelled)
130. (Previously presented) A method for preventing and/or reducing the growth of tumor cells in a patient, said method comprising the steps of administering a therapeutically effective amount of the oligonucleotide moiety of of claim 85 and a therapeutically effective amount of a purified protein capable of binding with said protein binding site to said patient.
131. (Original) The method of claim 130, wherein said tumor cells are selected from the group consisting of lung cancer cells, liver cancer cells, pancreatic cancer cells, brain cancer cells, colon cancer cells, kidney cancer cells, bone cancer cells, breast cancer cells, prostate cancer cells, uterine cancer cells, lymphoma cells, melanoma cells, myeloma

cells, adenocarcinoma cells, thymoma cells and plasmacytoma cells.

132-137. (Cancelled)

138. (Previously presented) A composition comprising the oligonucleotide moiety of claim 85 in association with a pharmaceutically acceptable carrier.

139. (Currently amended) The method of claim 85 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~covalently attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

140. (Currently amended) The method of claim 104 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~covalently attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

141. (Currently amended) The method of claim 107 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~covalently attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

142. (Currently amended) The method of claim 108 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~covalently attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

143. (Currently amended) The method of claim 109 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is

~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

144. (Currently amended) The method of claim 116 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.
145. (Currently amended) The method of claim 123 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.
146. (Currently amended) The method of claim 130 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.
147. (Currently amended) The method of claim 108 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.
148. (Currently amended) The composition of claim 138 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is ~~evaluating-attached~~ bound to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.